Athira PHARMA

ACT-AD Topline Results

Investor Webinar
June 22, 2022

ADVANCING NEW THERAPIES FOR NEURONAL HEALTH

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ACT-AD Topline Results

Hans Moebius, M.D., Ph.D.
Chief Medical Officer

ACT-AD Executive Summary

Proof of concept ACT-AD trial (N=77) provides important insights for further fosgonimeton development program

- Phase 1b study conducted with fosgonimeton as a monotherapy; Phase 2 allowed for add-on standard of care (AChEIs) to obtain safety data in a more representative real-world patient population
- Primary analysis not statistically significant; fosgonimeton suggests potentially beneficial treatment effect as a monotherapy
- By pre-specified analysis, fosgonimeton and background standard of care both showed positive treatment effects in ERP P300 latency and ADAS-Cog11 as monotherapies, but not in combination
- By post hoc analysis, the parallel ERP P300 latency (-28 ms) and ADAS-Cog11 (-3.3 points) signals appear more pronounced in fosgonimeton monotherapy
- Treatment with fosgonimeton was well tolerated, without typical CNS adverse effects, and safety profile was favorable
- Results will help inform LIFT-AD and optimize chances for success

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Fosgonimeton Phase 2 Trial (ACT-AD)

PROOF-OF-CONCEPT TRIAL TO HELP BETTER UNDERSTAND NATURE OF NOVEL INTERVENTION

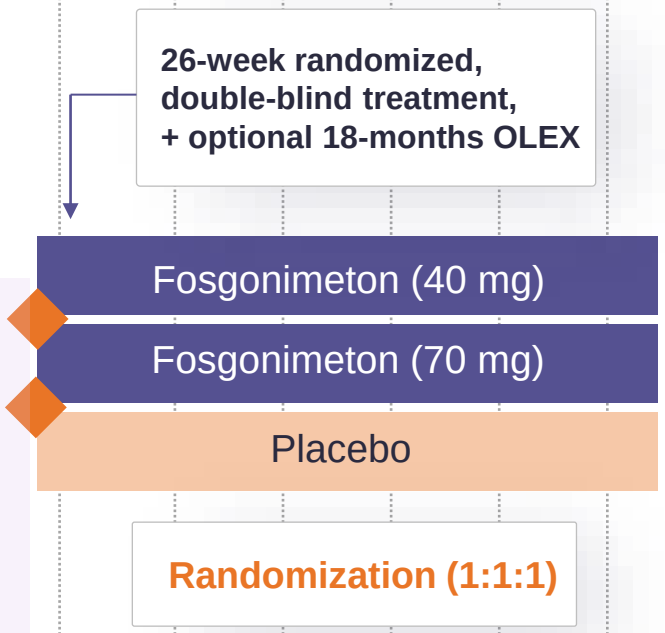
POPULATION

ACT-AD: N=77 (recruitment complete) mild-to-moderate AD dementia subjects
(55-85 years; CDR 1 and 2; MMSE 14-24 incl.)

Potential Pathways to success:

- Achieves statistical significance on primary endpoint
- Key secondary endpoints trending
- Functions as "interim analysis" for LIFT-AD without statistical penalty

TREATMENT DURATION



ENDPOINTS AND TIMELINE

PRIMARY ENDPOINT

- Change of P300 latency
- Safety

SECONDARY ENDPOINTS

- Cognition: ADAS-Cog11
- Global clinical change: ADCS CGIC - Clinician
- Function: ADCS-ADL23
- Plasma PK

Phase 2 ACT-AD: baseline demographics

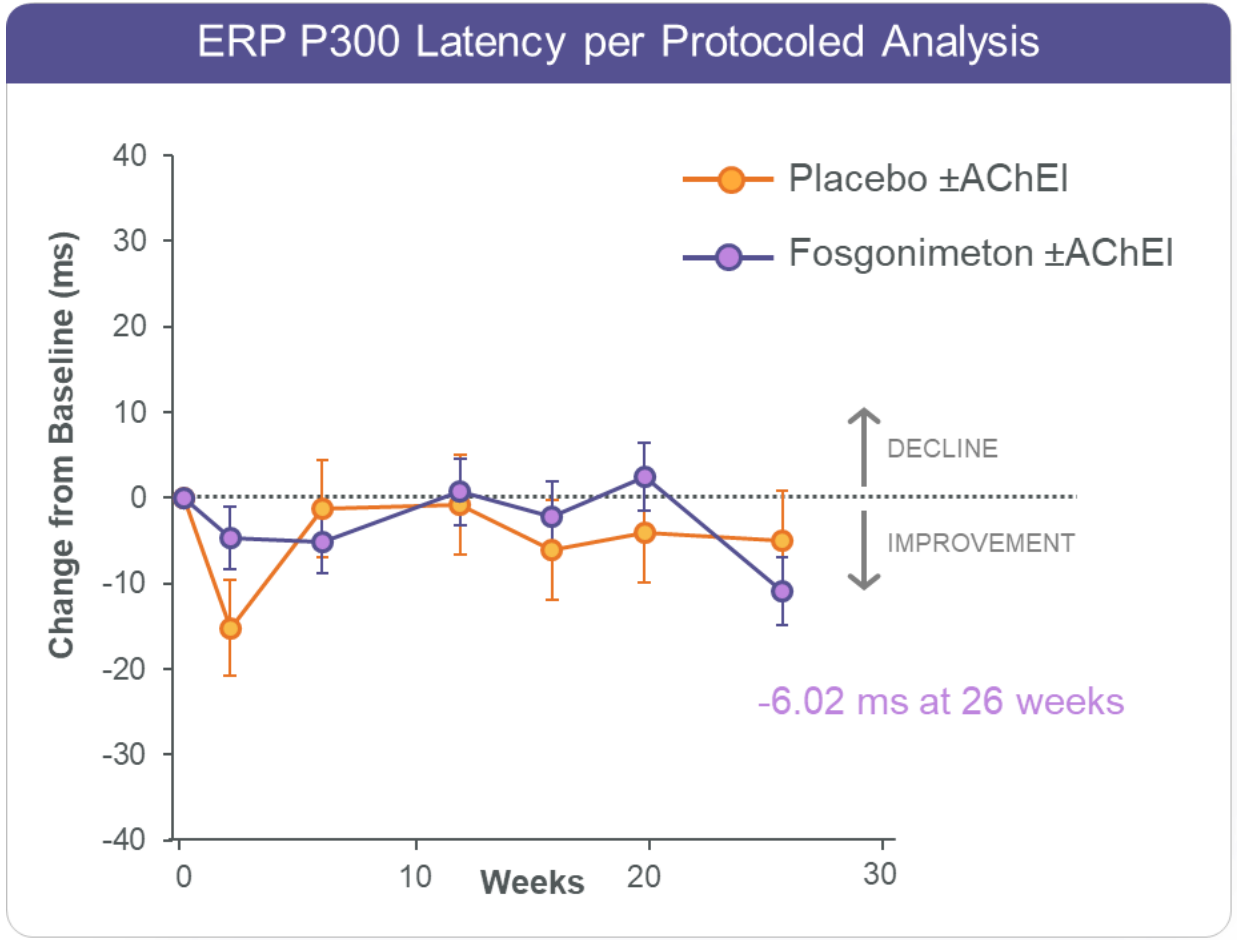
Baseline demographics consistent with appropriate mild-to-moderate Alzheimer's population

	Overall (N = 77)
Age at informed consent (years); mean (SD)	71.4 ± 7.3
Body mass index (kg/m^2), mean (SD)	25.4 ± 3.7
Sex, n (%)	
Female	39 (50.6%)
Male	38 (49.4%)
Years of education, mean (SD)	14.9 ± 2.8
Baseline MMSE, mean (SD)	19.0 ± 2.9
Concomitant AChEI, n (%)	47 (61%)
P300 Latency (SD)	376 ± 38.8

AChEi, acetylcholinesterase inhibitor; AD, Alzheimer's disease; MMSE, Mini-Mental State Examination; SD, standard deviation.

Primary endpoint of a statistically significant change in biomarker ERP P300 latency was not met

Modified intent to treat (mITT) population by a mixed model repeated measures (MMRM) analysis



	Visit	W2	W6	W12	W16	W20	W26
Placebo ±AChEI	CFB	-15.22	-1.26	-0.75	-6.06	-4.01	-4.95
	SE	5.582	5.601	5.817	5.812	5.912	5.839
	N	23	23	21	21	20	21

	Visit	W2	W6	W12	W16	W20	W26
Fosgonimeton ±AChEI	CFB	-4.75	-5.08	0.74	-2.13	2.50	-10.97
	SE	3.649	3.717	3.902	4.021	3.983	3.965
	N	50	48	44	40	41	41

	W2	W6	W12	W16	W20	W26
MMRM p-values	0.124	0.579	0.837	0.588	0.373	0.406

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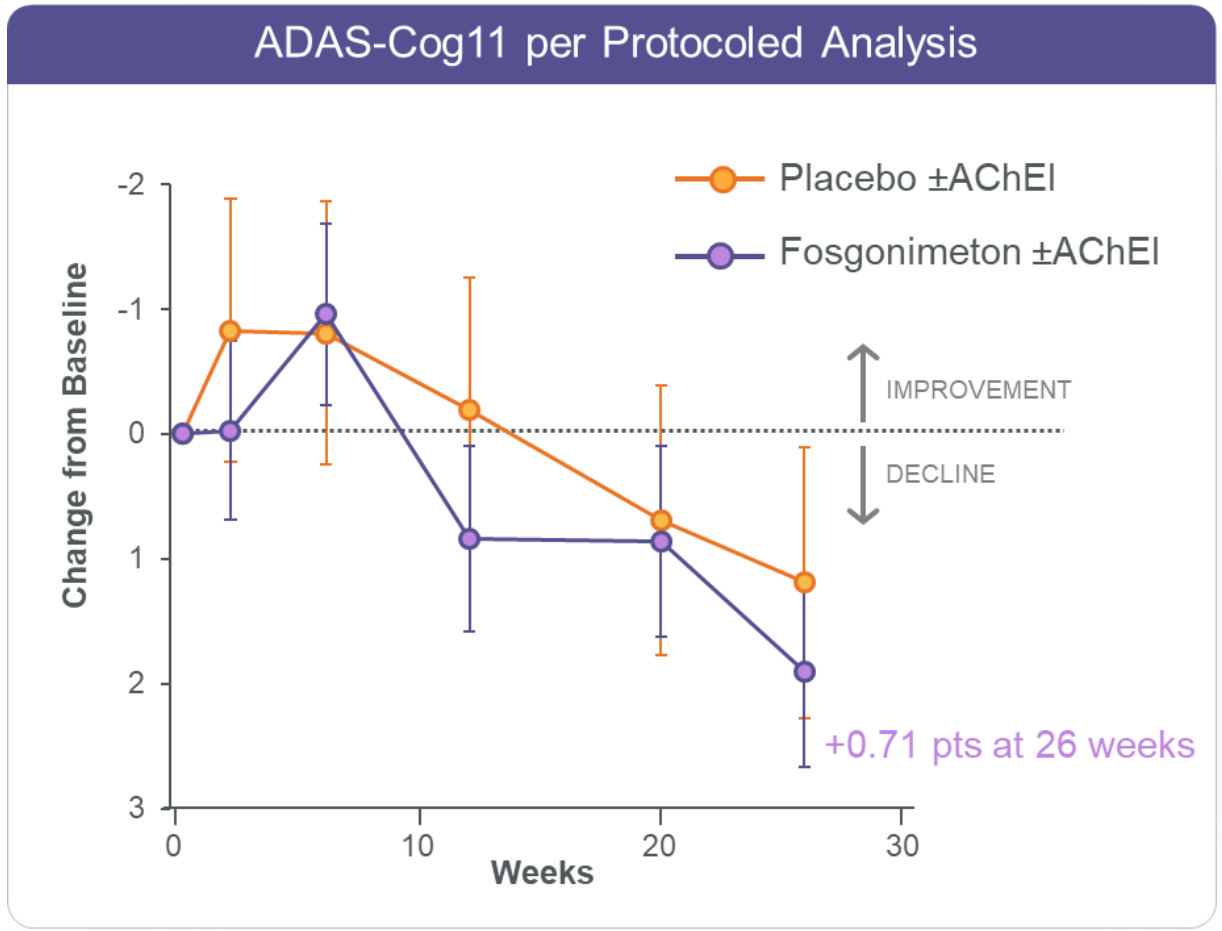
Data plotted as LS mean ± SE

No signal identified in key secondary endpoint of ADAS-Cog11

Modified intent to treat (mITT) population by a mixed model repeated measures (MMRM) analysis



	Visit	W2	W6	W12	W20	W26
Placebo ±AChEI	CFB	-0.83	-0.81	-0.19	0.69	1.19
	SE	1.052	1.052	1.067	1.083	1.082
	N	23	23	22	21	21

	Visit	W2	W6	W12	W20	W26
Fosgonimeton ±AChEI	CFB	-0.03	-0.96	0.84	0.86	1.9
	SE	0.716	0.724	0.745	0.761	0.763
	N	50	48	44	41	41

	W2	W6	W12	W20	W26
MMRM p-values	0.514	0.9032	0.407	0.888	0.577

Data plotted as LS mean ± SE

Subgroup analysis was performed per protocoled SAP

Pre-specified subgroup analysis suggested differential effects with concomitant standard of care

- Severity (mild or moderate)
- ApoE (carriers or non-carriers)
- AChEI use (+/- current use of acetylcholinesterase inhibitors including donepezil, rivastigmine, or galantamine)

- Analysis of the subgroups suggest AChEI use may impact outcomes
- No notable patterns observed in other subgroups to date

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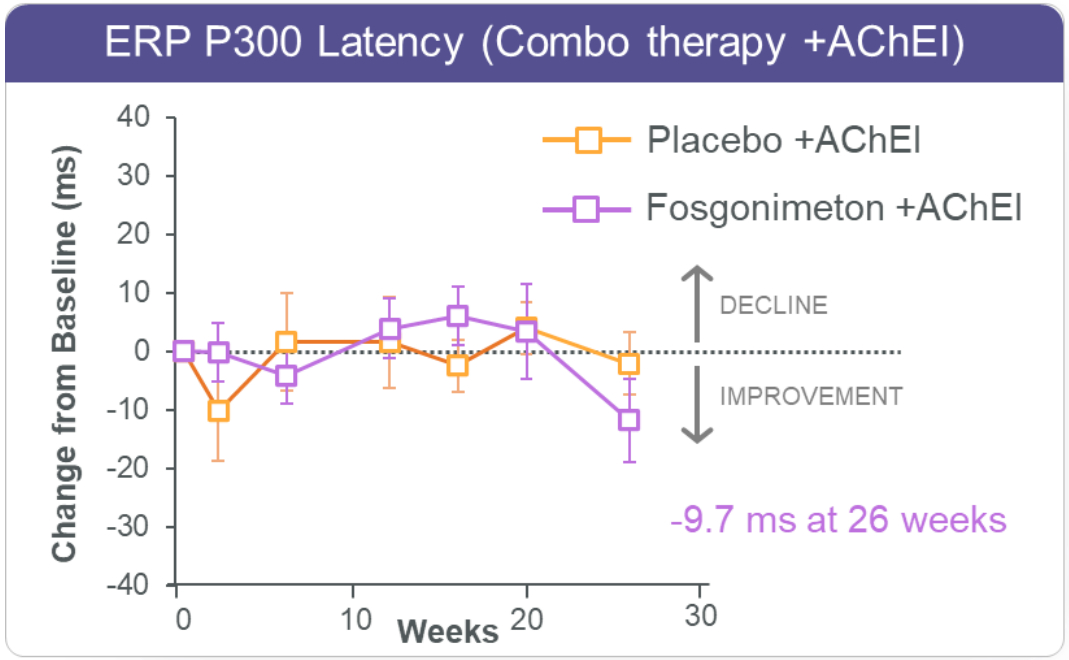
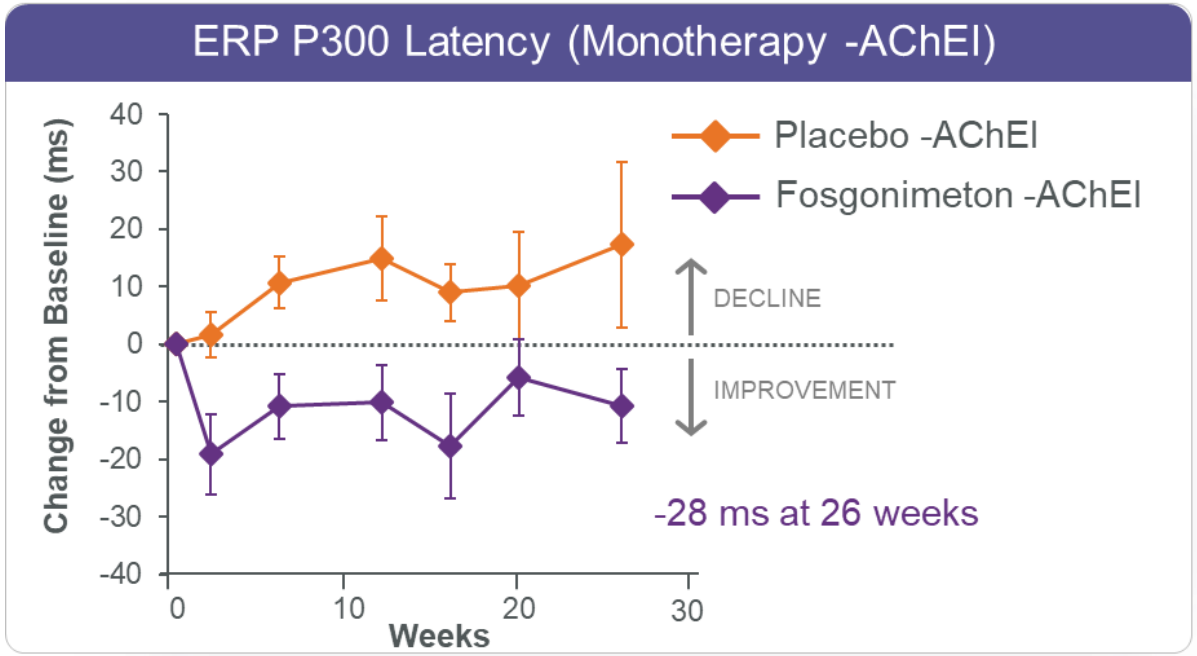
Subgroup analysis suggests differential ERP P300 latency effect

Modified intent to treat (mITT) population by Wilcoxon analysis





	Visit	W2	W6	W12	W16	W20	W26
Placebo +AChEI	CFB	-10.2	1.6	1.5	-2.5	4.0	-2.1
	SD	32.97	32.03	30.3	17.38	16.07	20.87
	SEM	8.51	8.27	7.82	4.49	4.46	5.39
	N	15	15	15	15	13	15

	Visit	W2	W6	W12	W16	W20	W26
Fosgonimeton +AChEI	CFB	-0.3	-4.2	3.9	6	3.4	-11.8
	SD	27.31	25.6	25.83	25.29	40.28	34.71
	SEM	4.99	4.75	5.07	5.06	8.06	7.09
	N	30	29	26	25	25	24
Wilcoxon p-values		0.3539	0.7289	0.6357	0.0993	0.5182	0.3193

	Visit	W2	W6	W12	W16	W20	W26
Placebo -AChEI	CFB	1.7	10.7	14.9	9.0	10.2	17.3
	SD	11.27	12.88	17.76	12.13	24.57	35.4
	SEM	3.98	4.55	7.25	4.95	9.29	14.45
	N	8	8	6	6	7	6

	Visit	W2	W6	W12	W16	W20	W26
Fosgonimeton -AChEI	CFB	-19.1	-10.8	-10.1	-17.6	-5.8	-10.7
	SD	31.13	24.3	27.83	35.34	26.35	26.71
	SEM	6.96	5.57	6.56	9.12	6.59	6.48
	N	20	19	18	15	16	17
Wilcoxon p-values		0.0565	0.024	0.0255	0.0216	0.2703	0.1952

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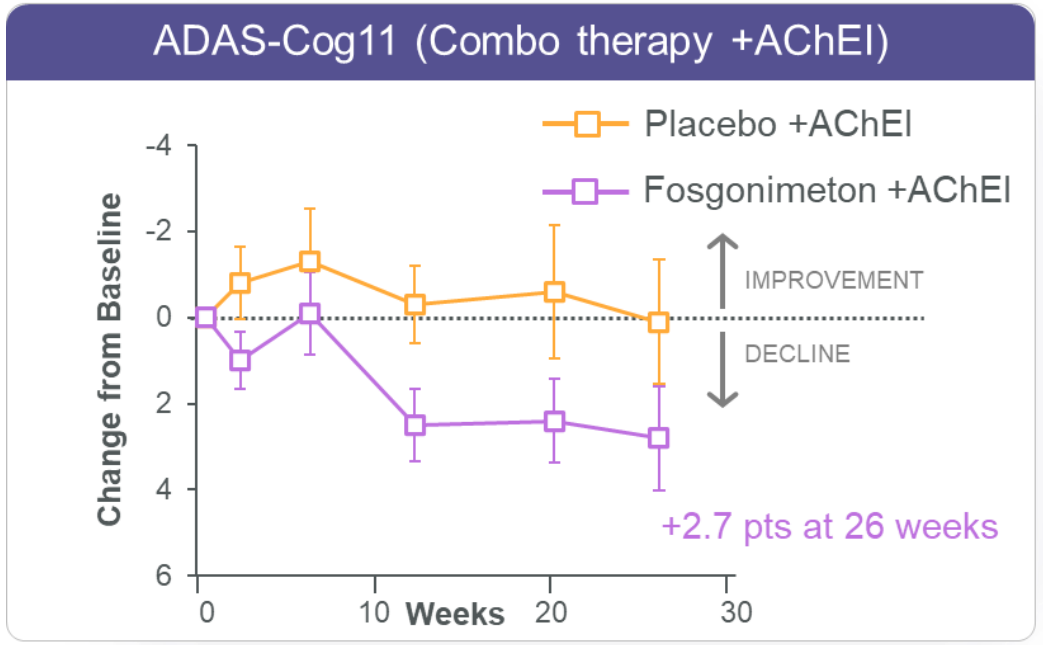
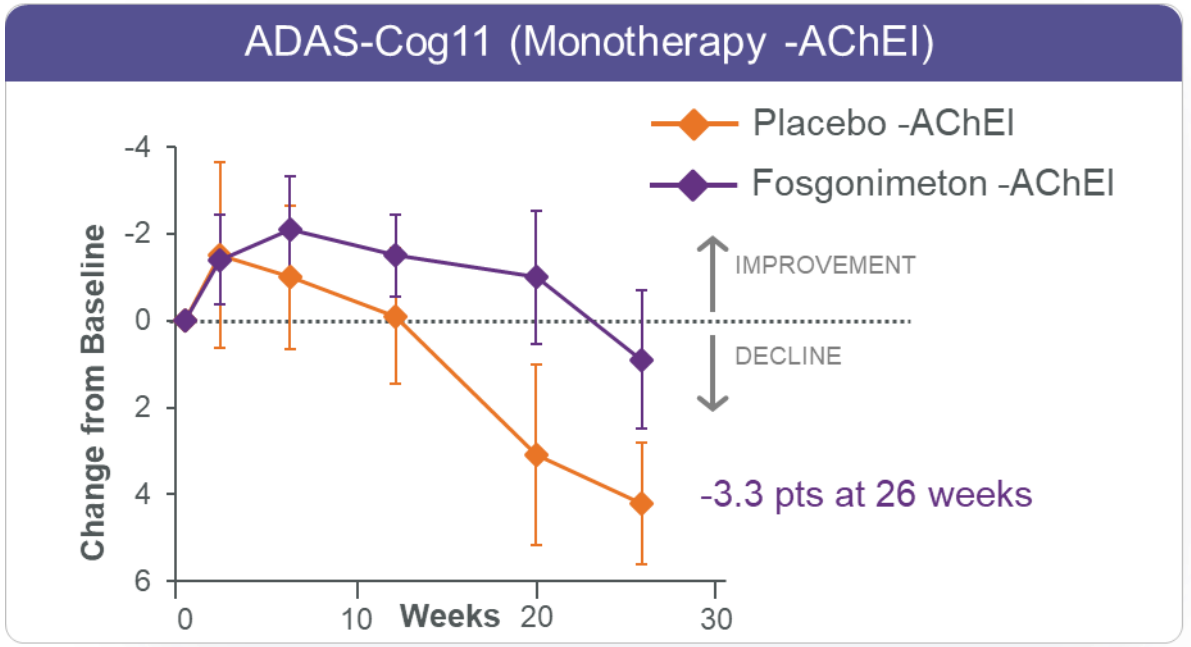
Data presented as unadjusted mean ± SEM

Subgroup analysis suggests differential ADAS-Cog11 effect

Modified intent to treat (mITT) population by Wilcoxon analysis





	Visit	W2	W6	W12	W20	W26
Placebo +AChEI	CFB	-0.8	-1.3	-0.3	-0.6	0.1
	SD	3.28	4.78	3.52	5.79	5.62
	SEM	0.85	1.23	0.91	1.55	1.45
	N	15	15	15	14	15

	Visit	W2	W6	W12	W20	W26
Fosgonimeton +AChEI	CFB	1.0	-0.1	2.5	2.4	2.8
	SD	3.6	5.09	4.23	4.75	5.79
	SEM	0.66	0.96	0.83	0.97	1.21
	N	30	28	26	24	23
Wilcoxon p-values		0.1567	0.6266	0.04	0.0919	0.3157

	Visit	W2	W6	W12	W20	W26
Placebo -AChEI	CFB	-1.5	-1.0	-0.1	3.1	4.2
	SD	6.05	4.69	4.14	5.49	3.43
	SEM	2.14	1.66	1.56	2.08	1.40
	N	8	8	7	7	6

	Visit	W2	W6	W12	W20	W26
Fosgonimeton -AChEI	CFB	-1.4	-2.1	-1.5	-1.0	0.9
	SD	4.6	5.45	4.03	6.3	6.74
	SEM	1.03	1.22	0.95	1.53	1.59
	N	20	20	18	17	18
Wilcoxon p-values		0.6827	0.6643	0.4647	0.0642	0.1412

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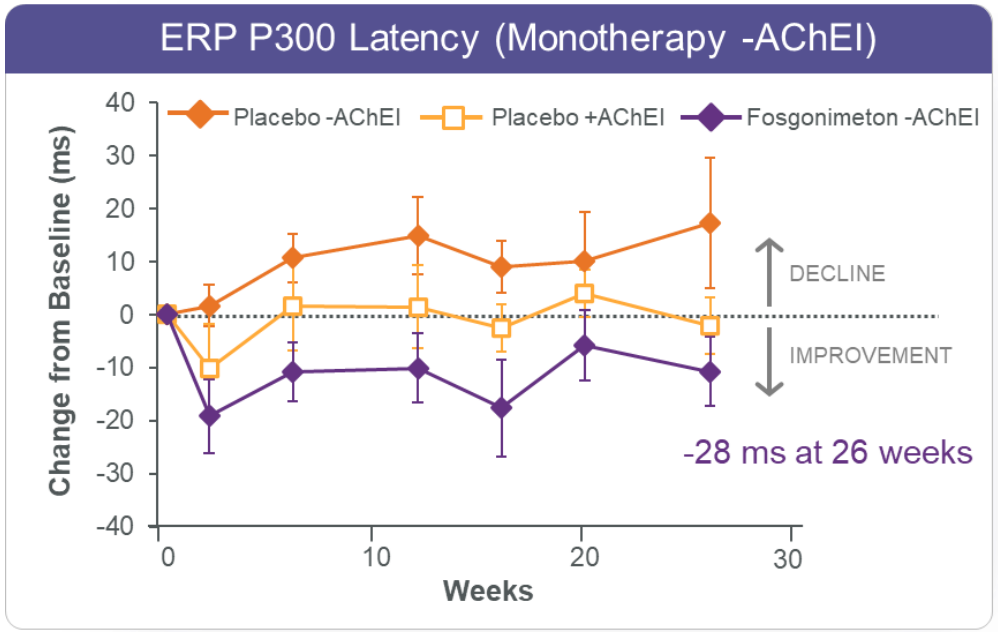
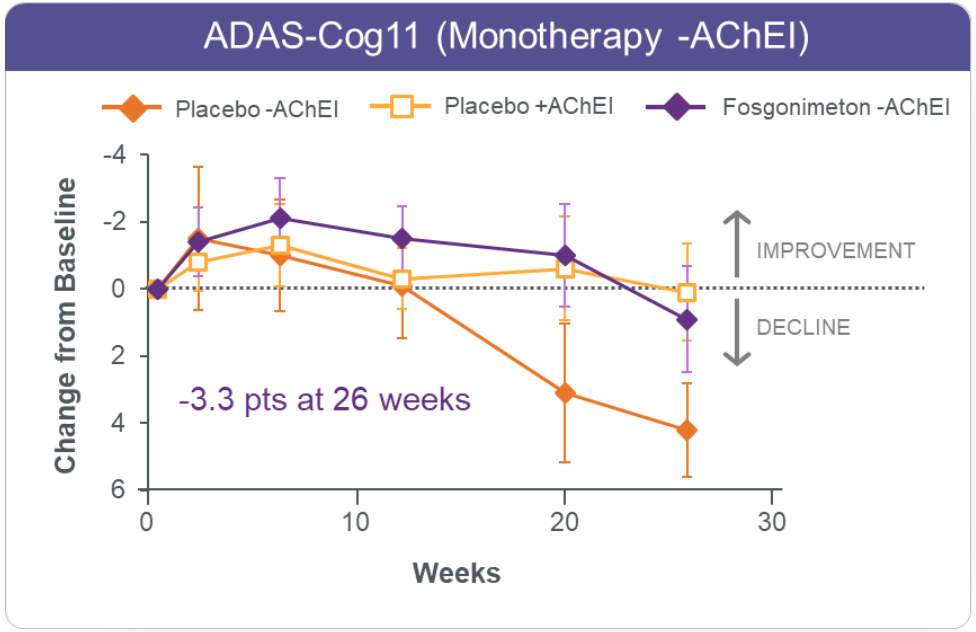
Data presented as unadjusted mean ± SEM

Fosgonimeton and standard of care monotherapy suggests positive treatment effects in ERP P300 latency and ADAS-Cog11

AChEI and placebo effects consistent with published literature; provide external validation of experiment





	Visit	W2	W6	W12	W16	W20	W26
Placebo -AChEI	CFB	1.7	10.7	14.9	9.0	10.2	17.3
	SD	11.27	12.88	17.76	12.13	24.57	30.15
	N	8	8	6	6	7	6

	Visit	W2	W6	W12	W16	W20	W26
Placebo +AChEI	CFB	-10.2	1.6	1.5	-2.5	4.0	-2.1
	SD	32.97	32.03	30.3	17.38	16.07	20.87
	N	15	15	15	15	13	15

	Visit	W2	W6	W12	W16	W20	W26
Fosgonimeton -AChEI	CFB	-19.1	-10.8	-10.1	-17.6	-5.8	-10.7
	SD	31.13	24.3	27.83	35.34	26.35	26.71
	N	20	19	18	15	16	17

	Visit	W2	W6	W12	W20	W26
Placebo -AChEI	CFB	-1.5	-1.0	-0.1	3.1	4.2
	SD	6.05	4.69	4.14	5.49	3.43
	N	8	8	7	7	6

	Visit	W2	W6	W12	W20	W26
Placebo +AChEI	CFB	-0.8	-1.3	-0.3	-0.6	0.1
	SD	3.28	4.78	3.52	5.79	5.62
	N	15	15	15	14	15

	Visit	W2	W6	W12	W20	W26
Fosgonimeton -AChEI	CFB	-1.4	-2.1	-1.5	-1.0	0.9
	SD	4.6	5.45	4.03	6.3	6.74
	N	20	20	18	17	18

Modified intent to treat (mITT) population by Wilcoxon analysis

Treatment with fosgonimeton was generally well tolerated with a favorable safety profile

VARIABLE	Placebo (N=24) N (%)	40mg Fosgonimeton (N=27) N (%)	70mg Fosgonimeton (N=26) N (%)	Overall (N=77) N (%)
Treatment Emergent AEs (TEAEs)	17 (70.8%)	24 (88.9%)	26 (100.0%)	67 (87.0%)
Treatment-Related TEAEs	8 (33.3%)	23 (85.2%)	24 (92.3%)	55 (71.4%)
Serious TEAEs	0 (0.0%)	3 (11.1%)	0 (0.0%)	3 (3.9%)
Treatment-Related Serious TEAEs	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Deaths	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TEAEs Leading to Study Drug Withdrawal	0 (0.0%)	4 (14.8%)	5 (19.2%)	9 (11.7%)
TEAEs Leading to Study Drug Interruption	0 (0.0%)	3 (11.1%)	3 (11.5%)	6 (7.8%)

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Safety population analysis

Fosgonimeton Phase 3 Trial (LIFT-AD)

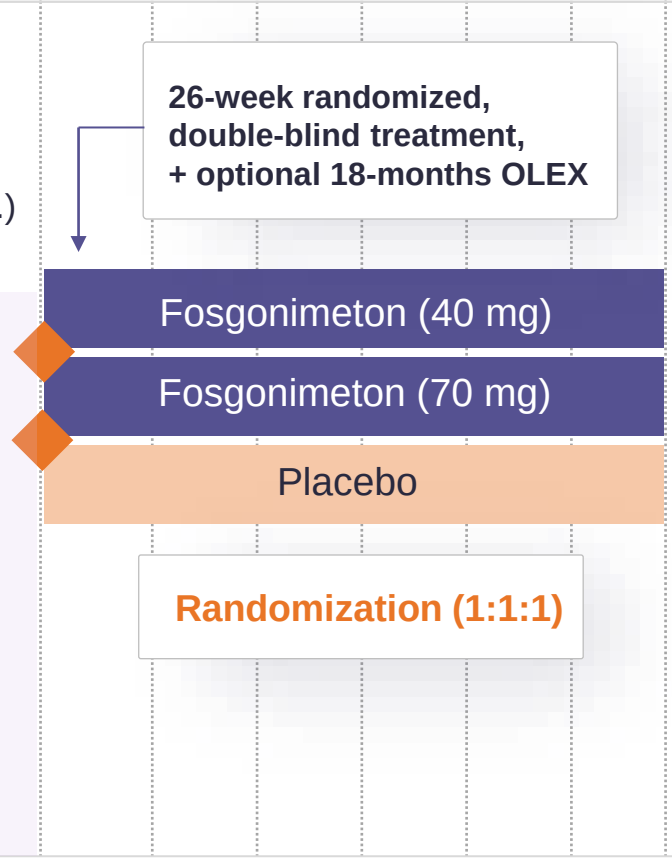
POPULATION

LIFT-AD: Target N=~420
mild-to-moderate AD dementia subjects
(55-85 years; CDR 1 and 2; MMSE 14-24 incl.)

Potential Pathways to success:

- Achieves statistical significance on primary endpoint
- Achieves statistical significance on two key secondary endpoints, which may support approval with a single pivotal study

TREATMENT DURATION



ENDPOINTS AND TIMELINE

PRIMARY ENDPOINT

- Global Statistical Test (GST) – unbiased composite, fed by data from two key secondaries
- Safety

SECONDARY ENDPOINTS

- Cognition: ADAS-Cog11
- Global clinical change: ADCS CGIC - Clinician
- Function: ADCS-ADL23

STATUS

- Enrollment underway
- Analysis to inform decision-making

Over 200 completing at least 20 weeks of treatment; ~50% monotherapy

ACT-AD Conclusion

This first small interventional trial with the positive HGF/MET modulator fosgonimeton supports its potential in Alzheimer's disease

- Primary analysis not statistically significant; fosgonimeton suggests potentially beneficial treatment effect as a monotherapy
- By pre-specified analysis, background AChEIs and fosgonimeton both showed positive treatment effects in P300 latency and ADAS-Cog11 as monotherapies, but not in combination
- By post hoc analysis, the parallel P300 latency (-28 ms) and ADAS-Cog11 (-3.3 points) signal appears more pronounced in fosgonimeton monotherapy
- Treatment with fosgonimeton was well tolerated, without typical CNS adverse effects, and safety profile was favorable
- Full analysis is ongoing
- The results will inform the optimization of the parallel Phase 3 LIFT-AD study, with over 200 completing at least 20 weeks of treatment; ~50% monotherapy
- Will seek advice from experts, advisors, and regulators on how to expeditiously analyze and potentially adapt the LIFT-AD study
- Recruitment to LIFT-AD and the transitions to the Open Label Extension study will continue

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Conclusion

Mark Litton, Ph.D.
Chief Executive Officer

Closing: Fosgonimeton has potential in Alzheimer's Disease

ACT-AD results to benefit LIFT-AD probability of success

- ACT-AD is the first study to show potential cognitive improvement with ADAS-Cog11 in AD patients by positive modulation of the HGF/MET receptor by fosgonimeton
- ACT-AD outcomes support our conviction that we have a unique opportunity to make a positive difference for patients suffering from neurodegenerative diseases
- ACT-AD results are important data that warrant further evaluation and inform how best to optimize the parallel LIFT-AD study
- Planned near term LIFT-AD analysis will also inform decision-making

Strong balance sheet to support fosgonimeton development program through key inflection points

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